

10/527481

PATENT COOPERATION TREATY



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INTERNATIONAL PRELIMINARY EXAMINATION REPORT

(PCT Article 36 and Rule 70)

REC'D 16 NOV 2004

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Applicant's or agent's file reference LLK/P33107	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/PEA416)	
International application No. PCT/EP 03/10261	International filing date (day/month/year) 10.09.2003	Priority date (day/month/year) 12.09.2002
International Patent Classification (IPC) or both national classification and IPC A61K31/4439		
Applicant GLAXO GROUP LIMITED et al.		
<p>1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.</p> <p>2. This REPORT consists of a total of 6 sheets, including this cover sheet.</p> <p><input type="checkbox"/> This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).</p> <p>These annexes consist of a total of sheets.</p> <p style="text-align: right;">EPO - DG 1</p>		
<p>3. This report contains indications relating to the following items:</p> <p style="text-align: right;">10. 12. 2004</p> <p style="text-align: center;">(52)</p> <p>I <input checked="" type="checkbox"/> Basis of the opinion</p> <p>II <input type="checkbox"/> Priority</p> <p>III <input checked="" type="checkbox"/> Non-establishment of opinion with regard to novelty, inventive step and industrial applicability</p> <p>IV <input type="checkbox"/> Lack of unity of invention</p> <p>V <input checked="" type="checkbox"/> Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement</p> <p>VI <input type="checkbox"/> Certain documents cited</p> <p>VII <input type="checkbox"/> Certain defects in the international application</p> <p>VIII <input type="checkbox"/> Certain observations on the international application</p>		
Date of submission of the demand 22.03.2004	Date of completion of this report 12.11.2004	
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80288 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Authorized Officer Hornich, E Telephone No. +49 89 2399-8721 	

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I. Basis of the report

1. With regard to the elements of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, Pages

1-8 as originally filed

Claims, Numbers

1-11 as originally filed

2. With regard to the language, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any nucleotide and/or amino acid sequence disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:
- ☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)).

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

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III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application,

☒ claims Nos. 1-8 (with regard to industrial applicability)

because:

☒ the said international application, or the said claims Nos. 1-8 (with regard to industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos.

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the Standard.

☐ the computer readable form has not been furnished or does not comply with the Standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Yes: Claims	2, 3, 8
	No: Claims	1, 4-7, 9-11
Inventive step (IS)	Yes: Claims	
	No: Claims	1-11
Industrial applicability (IA)	Yes: Claims	9-11
	No: Claims	

2. Citations and explanations

see separate sheet

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SECTION III

1. Claims 1-8 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

SECTION V

2. References:

- 2.1 D1: WO 02/08221 A
D2: WO 02/16317 A
D3: WO 99/63986 A
D4: BORTOLOTTI M ET AL: "The treatment of functional dyspepsia with red pepper" ALIMENTARY PHARMACOLOGY AND THERAPEUTICS, vol. 16, no. 6, June 2002 (2002-06), pages 1075-1082, ISSN: 0269-2813.
D5: LAZZERI M ET AL: "Intravesical capsaicin for treatment of severe bladder pain: A randomized placebo controlled study" JOURNAL OF UROLOGY, vol. 156, no. 3, 1996, pages 947-952, ISSN: 0022-5347.

2.2 Certain published documents (Rule 70.10)

Application No Patent No	Publication date (day/month/year)	Filing date (day/month/year)	Priority date (valid claim) (day/month/year)
WO 03/022809	20/03/03	13/09/02	13/09/01
WO 03/053945	03/07/03	19/12/02	20/12/01
WO 03/068749	21/08/03	13/02/03	15/02/02
WO 02/072536	19/09/02	07/03/02	09/03/01
WO 02/090326	14/11/02	02/05/02	02/05/01

The above-mentioned documents were *published between the priority date and the filing date* of the present application.

On the assumption that the *priority* of the present application has been **validly claimed**, the above-mentioned documents are presently *not considered prior art* (R. 33.1 and 64.1 PCT).

The above-mentioned documents disclose the use of vanilloid receptor antagonists for the treatment of the diseases referred to in the present application.

3. Novelty (Art. 33(2) PCT)

3.1 D1 discloses compounds acting as vanilloid receptor antagonists (Type I). The compounds are useful for the treatment of pain of various origin, e.g. gas pains, menstrual pain or bladder hypersensitivity.

D1 would appear to be **prejudicial** to the novelty of claims 1, 7 and 9-11.

3.2 D2 discloses thiocarbamic acid derivatives being vanilloid receptor antagonists. The compounds are useful in treatment of pain, e.g. urinary bladder hypersensitiveness, irritable bowel syndrome or inflammatory bowel disease. Irritable Bowel Syndrome (IBS) is part of a spectrum of diseases known generally as Functional Gastrointestinal Disorders which include diseases such as non-cardiac chest pain, abdominal pain and non-ulcer dyspepsia.

D2 would **anticipate** the subject-matter of claims 1, 4, 7 and 9-11.

3.3 D3 relates to pharmaceutical compositions comprising e.g. capsaicin for the treatment of reflux oesophagitis, gastritis, dyspepsia or peptic ulceration. Gastro-oesophageal reflux disease includes reflux oesophagitis, gastritis, dyspepsia, peptic ulceration and/or Barrett's oesophagus.

D3 would **anticipate** the subject-matter of claims 1, 4-7 and 9-11.

3.4 D4 reports on the beneficial effects of red pepper/capsaicin on functional dyspepsia and pain associated therewith, e.g. heartburn. The disclosure of the document would **anticipate** the subject-matter of claims 1, 4, 5, 7 and 9-11.

3.5 D5 reports on capsaicin for the treatment of pelvic or bladder pain. D5 would take away the novelty of claims 1, 7 and 9-11.

4. Inventive Step (Art. 33(3) PCT)

According to the above-cited documents, the use of *vanilloid receptor antagonists* for the treatment of pain in the gastrointestinal tract are well known in the art. It would thus be obvious for the skilled person that the *vanilloid receptor antagonists* would as well

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be beneficial in the treatment of renal or biliary colic and pain associated therewith. The use of a particular *vanilloid receptor antagonist* according to claim 8 would not be considered of such a significance as to support an inventive step.

An *inventive step* could thus *not* be *acknowledged* for the subject-matter of claims 2, 3 and 8.

5. Industrial Applicability (Art. 33(4) PCT)

5.1 For the assessment of the present claims 1-8 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

5.2 The requirements of industrial applicability would be fulfilled for the subject-matter of claims 9-11.